REMARKS

Claims 1, 3, 7-15, and 17-19 and 21-45 were pending in the application. Claims 10-14, 18, 21, and 23-45 have previously been withdrawn. Claims 2, 4-6, 16, 20 and 46-47 have previously been canceled. Claims 1, 3, 7-15, 17-19, 21, and 22-45 are thus pending, with claims 1, 3, 7-9, 15, 17, 19, and 22 under examination. No new matter has been added.

Rejection of Claims 1, 3 and 22 Under 35 U.S.C. § 102(e)

Claims 1, 3 and 22 stand rejected under 35 U.S.C. § 102(e), as allegedly anticipated by Bonjouklian *et al.* (U.S. Patent No. 5,504,103). Specifically, the Examiner states that "Bonjouklian *et al*., teach methods of treating phsphatidylnositos-3-kinase [sic] dependent conditions in a mammal contacting the cell with wortmannin or wortmannin analog" (p. 3 of instant office action).

Applicant respectfully traverses the rejection. While the Examiner contends that, "it is inherent in the methods taught by Bonjouklian *et al*., that the administration…results in the inhibition of phosphatidylinositol-3-kinase" (p. 3 of instant Office Action), it is not inherent that such inhibition also inhibits T cell activation and production of IL-2 by a T cell. For instance, Harada *et al*. in 2001 (submitted herein in a Supplemental IDS), well after the priority and filing dates of both the instant application or Bonjouklian *et al*., state "[t]he role of PI3K in CD28 costimulation remains controversial…we conclude that PI3K is not absolutely required for CD28-mediated IL-2 gene transcription" (p. 9006, right col., 1st paragraph). They further state, "it was reported that wortmannin treatment did not decrease or, in some cases, even increased CD28-dependent co-stimulation of IL-2 production" (p. 9006, right col., 2nd paragraph). It is clear from Harada *et al*., that the state of the art well after the filing of the instant application and Bonjouklian *et al*., was that of uncertainty and ambiguity. Contrary to the Examiner's position, Bonjouklian *et al*., would not have inherently obtained an inhibition of T cell activation. The teachings of the instant disclosure and claimed methods are therefore novel. Applicant, therefore, respectfully requests reconsideration and withdrawal of the rejection.

Rejection of Claims 1, 15, 17, 19 and 22 Under 35 U.S.C. § 112, First Paragraph: Enablement

The Examiner has rejected claims 1, 15, 17, 19 and 22 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. Specifically, the Examiner contends that the specification, "does not reasonably provide enablement for claims directed to a method of inducing unresponsiveness to an antigen in a T cell with the intended use of treating a human subject suffering from an autoimmune disease" (p. 8 of the instant office action).

Applicant respectfully traverses the rejection. The Examiner states, "the specification teaches that a phosphtidylinoistol-3-kinase inhibitor can inhibit production of IL-2 induced by CD28 ligation and thus induces unresponsiveness to an antigen" (p. 9, 1st paragraph). Applicants request clarification as to why Claim 1 was rejected under 35 U.S.C. § 112, first paragraph and make note that Claim 1 was not rejected under 35 U.S.C. § 112, first paragraph, in the Final Office Action mailed December 13, 2007.

One of ordinary skill in the art would recognize and could induce unresponsiveness to an antigen in a T cell from the teachings of the instant specification. Moreover, it was well known in the art that the primary interaction between a T cell receptor complex and a major histocompatibility complex triggers an activation signal in the T cell. A costimulatory signal is also required (such as CD28) or T cell receptor signaling can induce a state of anergy. Provided this and the teachings of the instant application, one of ordinary skill would only have to perform routine experimentation to practice the invention. For instance, p. 9, lines 4-13 of the instant specification teaches induction of T cell unresponsiveness to an antigen or alloantigen. Immediately following this paragraph, the specification teaches induction of T cell unresponsiveness to an antigen *in vivo* (p. 9, lines 14-31). Given the *in vitro* data and results, including from Examples 1, 2 and 5 (pages 14-17, 18-19), only routine experimentation would be required for treating an autoimmune disease by administering T cells to a subject. Reconsideration and withdrawal of these rejections is, therefore, respectfully requested.

Rejection of Claims 1, 3, 7-9 Under Nonstatutory Obviousness-Type Double Patenting

Claims 1, 3, and 7-9 stand rejected on the grounds of nonstatutory obviousness-type double patenting, as allegedly being unpatentable over claims 1-4 and 7-10 of U.S. Patent No.

6,632,789. Applicant respectfully requests that the Examiner hold all nonstatutory obviousness-type double patenting rejection in abeyance, until allowable subject matter is determined.

CONCLUSION

Early and favorable consideration of the application is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at (617) 832-1000. If any fees are due, the Commissioner is hereby authorized to credit any overpayment or charge any deficiencies to **Deposit Account No. 06-1448, WYS-014.02**.

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Customer No.: 25181

Respectfully submitted,

By */DeAnn F. Smith/*
DeAnn F. Smith
Registration No.: 36,683
FOLEY HOAG LLP
155 Seaport Blvd
Boston, Massachusetts 02210
(617)832-1000
Attorney for Applicant